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Surgical Anterior Ventricular Endocardial Restoration (SAVER) in the Dilated Remodeled Ventricle After Anterior Myocardial Infarction

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OBJECTIVES The goal of this study was to evaluate the safety and efficacy of surgical anterior ventricular endocardial restoration (SAVER). The procedure excludes noncontracting segments in the dilated remodeled ventricle after anterior myocardial infarction.

BACKGROUND Anterior infarction leads to change in ventricular shape and volume. In the absence of reperfusion, dyskinesia develops. Reperfusion by thrombolysis or angioplasty leads to akinesia. Both lead to congestive heart failure by dysfunction of the remote muscle. The akinetic heart rarely undergoes surgical repair.

METHODS A new international group of cardiologists and surgeons from 11 centers (RESTORE group) investigated the role of SAVER in patients after anterior myocardial infarction. From January 1998 to July 1999, 439 patients underwent operation and were followed for 18 months. Early outcomes of the procedure and risk factors were investigated.

RESULTS Concomitant procedure included coronary artery bypass grafting in 89%, mitral valve (MV) repair in 22% and MV replacement in 4%. Hospital mortality was 6.6%, and few patients required mechanical support devices such as intraaortic balloon counterpulsation (7.7%), left ventricular assist device (0.5%) or extracorporeal membrane oxygenation (1.3%). Postoperatively, ejection fraction increased from 29 ± 10.4 to 39 ± 12.4%, and left ventricular end systolic volume index decreased from 109 ± 71 to 69 ± 42 ml/m^2 ($p < 0.005$). At 18 months, survival was 89.2%. Time related survival at 18 months was 84% in the overall group and 88% among the 421 patients who had coronary artery bypass grafting or MV repair. Freedom from readmission to hospital for congestive heart failure at 18 months was 85%. Risk factors for death at any time after the operation included older age, MV replacement and lower postoperative ejection fraction.

CONCLUSIONS Surgical anterior ventricular endocardial restoration is a safe and effective operation in the treatment of the remodeled dilated anterior ventricle after anterior myocardial infarction. (J Am Coll Cardiol 2001;37:1199–209) © 2001 by the American College of Cardiology

Myocardial infarction of the anterior wall leads to changes in ventricular shape and size (1,2). Dramatic improvement in regional left ventricular systolic function is not common after reperfusion therapy (3). There is loss of contraction of the anterior wall and septum. The remote muscle dilates as an adaptive mechanism to maintain stroke volume. Ventricular dysfunction occurs as a consequence of this remodeling and may lead to congestive heart failure (CHF).

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One large series examined the role of coronary artery bypass grafting (CABG) alone among patients with poor systolic function. Operative mortality was low and unrelated to (EF). However, among patients with EF <30%, five- and eight-year survivals were 65% and 45%, respectively (4).

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Another large study of CABG alone emphasized the importance of ventricular volume as an additional predictor of survival at five years. Patients with EF <30% had a five-year survival of 54% if the left ventricular end systolic volume index (LVESVI) was >100 ml/m^2. Among these survivors, two-thirds had CHF (5).

Traditional surgical methods reduce volume only if a dyskinetic scar is present. Surgical repair of the postinfarction dyskinetic dilated ventricle evolved from simple excision and closure (6) to Jatene's septal exclusion (7). Volume reduction was not considered for the akinetic segment. In 1984, Dor et al. (8) first recognized that the physiological consequences of akinesia and dyskinesia were similar in their adverse effect on global ventricular size and function. They devised a surgical procedure in conjunction with CABG to reduce ventricular volume. The operation reduces ventricular size by excluding the noncontracting segment with an intraventricular patch. Dor's procedure is applicable to both morphologies (9,10). Survival at eight years, including operative mortality in patients with severely depressed ventricular function (EF < 30%), was 69% (11).

The importance of volume reduction in the prognosis of

Abbreviations and Acronyms

CABG = coronary artery bypass grafting
CHF = congestive heart failure
CL = confidence limits
ECMO = extracorporeal membrane oxygenation
EF = ejection fraction
IABP = intraaortic balloon counterpulsation
LVAD = left ventricular assist device
LVESVI = left ventricular end systolic volume index
MV = mitral valve
SAVER = surgical anterior ventricular restoration

postinfarction patients with systolic dysfunction and ventricular dilation has been established. A group was assembled to verify Dor's operative experience in multiple centers and to assess intermediate clinical outcomes. The term "restoration" refers to surgical methods that reverse pathologic left ventricular remodeling (12). Surgical anterior ventricular restoration (SAVER) is an operation that reduces ventricular volume and utilizes Dor's principles with some technical modifications.

METHODS

Investigators. The Reconstructive Endoventricular Surgery, returning Torsion Original Radius Elliptical Shape to the LV (RESTORE) group (see Appendix for list of participating investigators) is an international team of cardiologists and surgeons from eleven institutions on four continents. We examined the role of SAVER in postinfarction dilation.

Patient population. From January 1998 to July 1999, RESTORE members performed SAVER in 439 patients for postinfarction dilated cardiomyopathy. Median time from infarction to operation was reported among 263 patients and was 564 days (25th percentile: 80 days, 75th percentile: 2,487 days.) Age ranged from 25 to 89 years (mean 63 ± 10.7). Akinesia was seen in 64% of patients (279 patients), dyskinesia in 33% (146 patients) and unstated in 3% (14 patients).

Variables included date of operation, concomitant procedures including CABG, mitral valve (MV) repair or mitral replacement, method of myocardial protection during the restoration phase of the procedure (cardioplegia vs. open-beating) and mechanical support modalities, including intraaortic balloon counterpulsation (IABP), left ventricular assist device (LVAD) and extracorporeal membrane oxygenation (ECMO). Preoperative and postoperative EF and LVESVI were measured. Postoperative New York Heart Association functional class and rehospitalizations for CHF were documented.

Surgical procedure. The SAVER portion of the operation is performed immediately after CABG and MV repair or replacement if indicated. During SAVER, the infarcted anterior wall segment is incised parallel to the left anterior descending artery. Internal inspection of the ventricle identifies scarred and viable myocardium. Transmural palpation of contracting muscle precisely delineates the junction of viable and nonviable tissue (Fig. 1). An encircling suture at this junction excludes the scar from the ventricular cavity and creates a pursed opening, usually about 2 by 3 cm (Fig. 2) (13). A dacron patch is secured onto this opening and eliminates the akinetic or dyskinetic segment (Fig. 3). Finally, the excluded scar is folded over the patch to assure hemostasis (Fig. 4).

Dor's patch insertion was described in the cardioplegia-arrested heart. Some members of the RESTORE team modified his myocardial protection method by using cardioplegia arrest during CABG/MV repair or replacement followed by open-beating technique during patch placement (14).

Statistics. Survival and freedom from rehospitalization were estimated both nonparametrically (15) and parametrically (16).

Univariable exploration of the association of variables with respect to death or rehospitalization included chi-square testing of frequency and Student *t* test for continuous variables. Correlations were sought between variables. Life tables stratified by categorical variables were compared by the log-rank test. Calibration of continuous variables was achieved by appropriate transformation of scale with the aid of decile risk analysis. Interaction terms were formed to identify differences in influence depending on myocardial protection method.

A directed technique of stepwise entry of variables was used (17). This was supplemented by bootstrap resampling, whereby 1,000 random samples of the data were drawn with replacement and an automated forward stepwise analysis performed with a p value criterion for retaining variables of 0.05. The relative frequency of occurrence of variables in these 1,000 models was used to inform the final selection of variables (18). The p value criterion for retention of variables in the final models was 0.1. Regression coefficients are presented ± 1 standard error.

The use of postoperative mechanical support was analyzed by logistic regression, using similar variable selection techniques.

Means are presented ± 1 standard deviation. Confidence limits (CL) of proportions, life table estimates and nomograms for multivariable analyses are asymptotic equivalents of one standard error.

RESULTS

Procedures. The SAVER procedure was carried out in all 439 patients. Concomitant CABG grafting was performed in 89% of operations, while mitral repair was used in 22% and mitral replacement in only 4%. Patients who underwent MV repair or replacement had lower preoperative EF (Fig. 5).

Efficacy of operation. Mean preoperative EF was 29 ± 10.4% and increased postoperatively to 39 ± 12.4% ($p <$

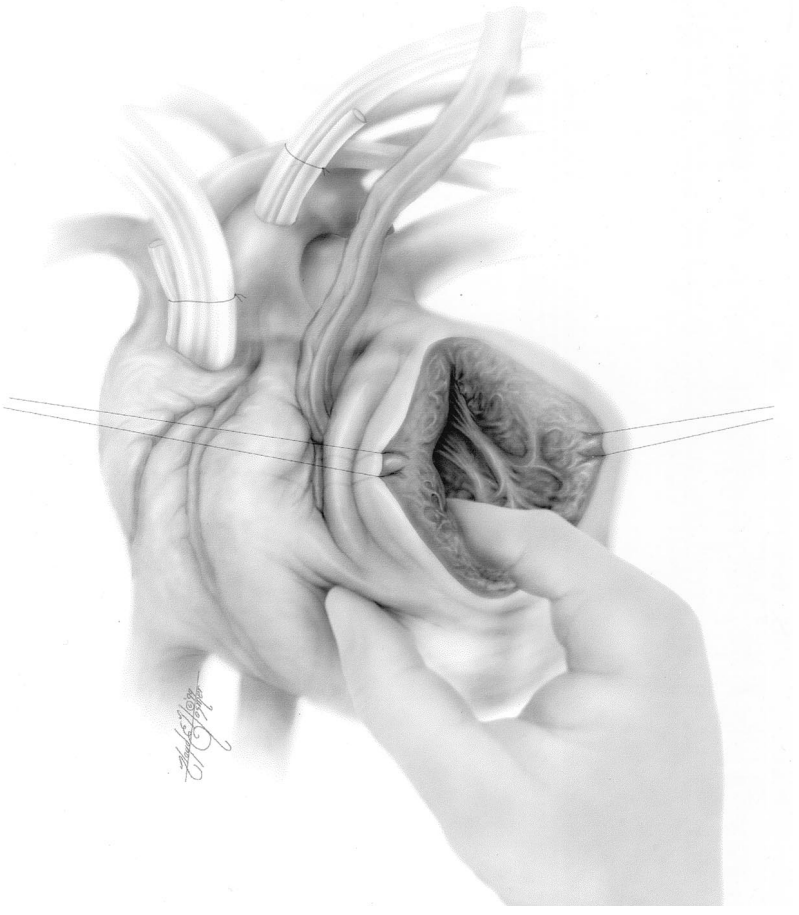

Figure 1. The anterior ventricular scar (akinesia or dyskinesia) is opened and inspected. Palpation of the open-beating heart precisely delineates the margins of contracting tissue. Reproduced with permission © 1999 Floyd E. Hosmer.

0.0001). Preoperative LVESVI, measured by ventriculography, averaged 109 ± 71 ml/m^2 and decreased postoperatively to 69 ± 42 ml/m^2 ($p < 0.0001$), a reduction of 41 ± 42 ml/m^2 (Table 1). Normal LVESVI is 24 ± 10 ml/m^2 (19).

Myocardial protection. Multivariable analysis has not shown a survival advantage with either type of myocardial protection in the overall population. Hospital mortality was 15 of 233 patients after cardioplegia arrested restoration (6.4%; CL: 4.8% to 8.6%) and was 14 of 204 (6.9%; CL: 5.0% to 9.2%) in patients receiving the open-beating technique ($p = 0.9$). Time related survival has also been similar ($p = 0.8$).

Postoperative mechanical support. In 439 operations, a small number of patients required IABP (7.7%), LVAD (0.05) or ECMO (1.3%) support. Multivariable logistic regression analysis showed that a concomitant MV repair/replacement or a lower postoperative EF predicted the need for support (Fig. 6). Preoperative EF did not predict the need for support.

Intraaortic balloon counterpulsation use among patients with preoperative EF <30% was related to intraoperative myocardial protection and suggests an advantage of the open-beating method of protection. This technique was used in one center during patch placement in 31 patients (14,20). Average preoperative EF was 20% and LVESVI

Table 1. Left Ventricular Volume and Function

			Percentiles						
Variable	**n**	**Mean ± SD**	**Min**	**10**	**25**	**50**	**75**	**90**	**Max**
Preoperative EF	411	29 ± 10	6	15	20	29	35	43	64
Postoperative EF	354	39 ± 12	9	24	30	40	48	55	75
Change in EF	349	11 ± 11	−20	−2	4	10	18	25	42
Preoperative LVESVI	185	109 ± 71	15	38	52	95	143	210	500
Postoperative LVESVI	191	69 ± 42	5	23	36	61	97	125	225
Change in LVESVI	166	−41 ± 42	−275	−87	−54	−32	−15	−4	39

EF = ejection fraction (%); LVESVI = left ventricular end systolic volume index (ml/m^2).

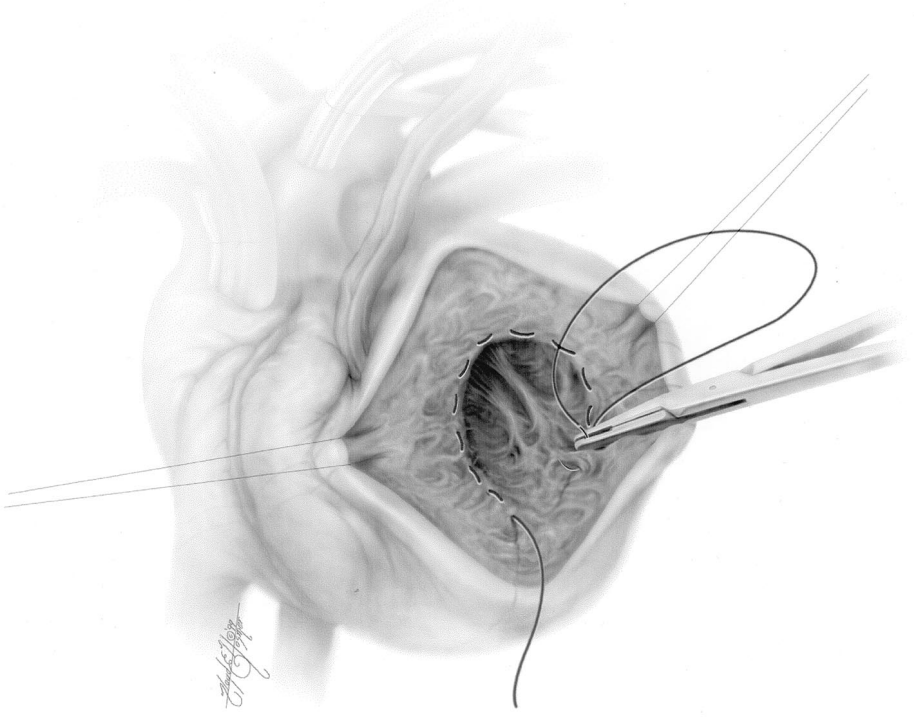

Figure 2. An encircling suture separates the viable myocardium from scar and when tightened forms an oval platform onto which a patch can be secured, usually 2 by 3 cm. Reproduced with permission © 1999 Floyd E. Hosmer.

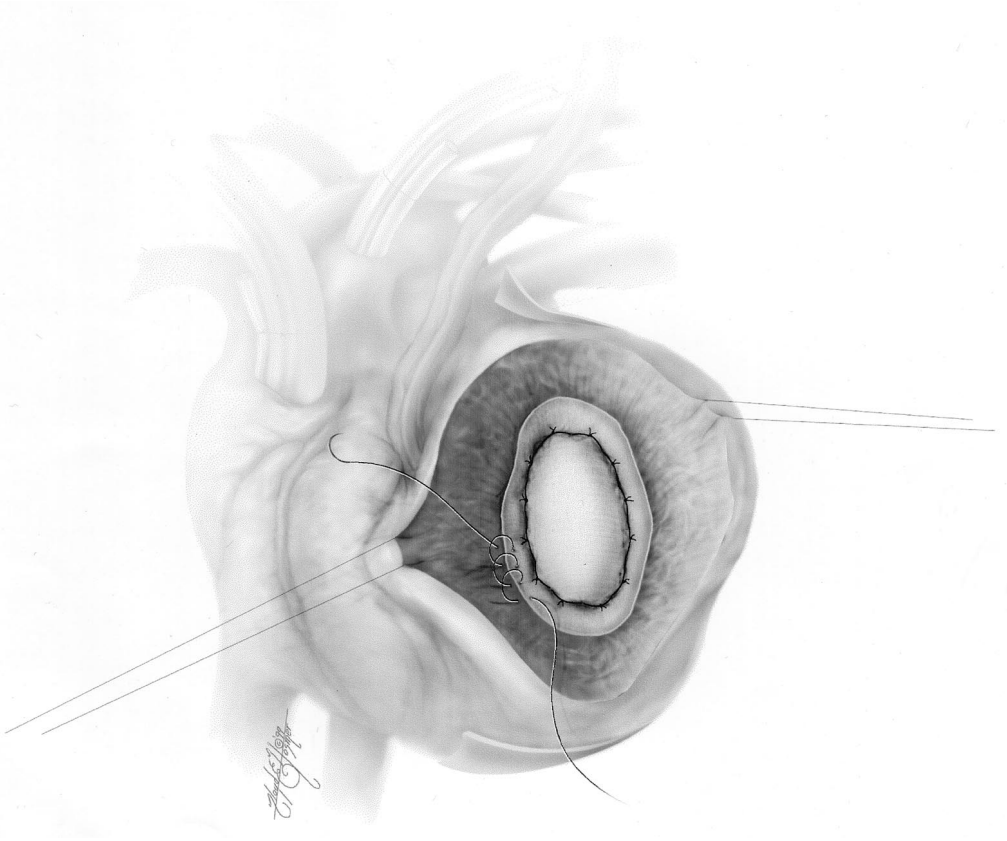

Figure 3. The dacron patch is sewn into place either by mattressed interrupted sutures brought from outside of the ventricle to its interior or by an internal continuous running stitch. Reproduced with permission © 1999 Floyd E. Hosmer.

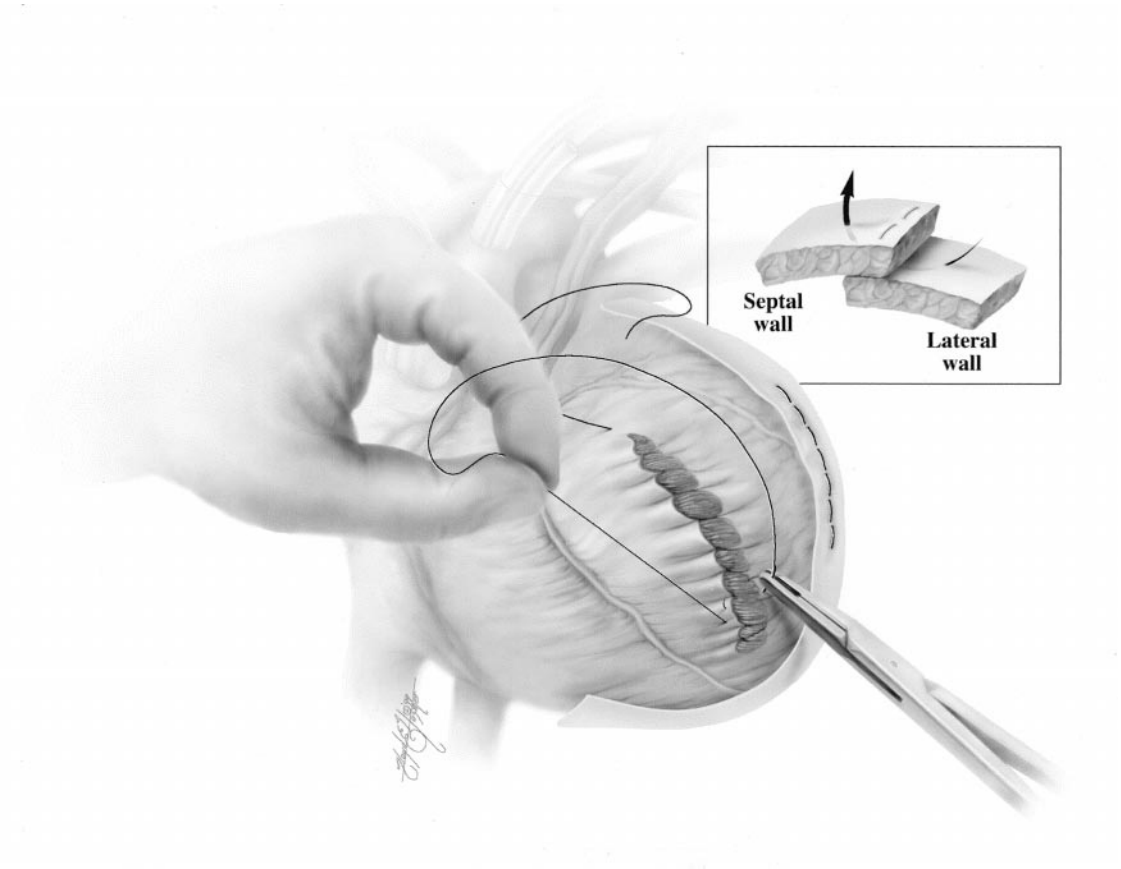

Figure 4. The remaining akinetic or dyskinetic noncontracting scar is sewn over the patch and aids in hemostasis. Reproduced with permission © 1999 Floyd E. Hosmer.

was 140 ml/m^2. Aortic occlusion time during CABG or mitral procedure averaged 87 min (range 60 to 140 min). Patients were weaned off bypass with minimal drug support (2.5 μg/kg/min dopamine), and only two patients required IABP support.

Another center in the RESTORE group used crystalloid cardioplegic arrest during CABG or mitral procedure throughout patch placement in 88 patients. Mean EF was 20% and LVESVI was 109 ml/m^2. Substantial inotropic support (epinephrine) and IABP use for low output were 15% and 40%, with aortic occlusion times of 50 and 100 min respectively.

Survival. Overall hospital mortality among the 439 patients was 6.6% (29 deaths). Mortality among 421 patients with CABG or MV repair was 5.1%. It was higher among 18 patients with CABG or MV replacement (28%, $p < 0.0001$).

Follow-up at 18 months revealed 17 late deaths. The risk of death was higher in the first month after operation but rapidly declined thereafter to a level of 6.5% per year by 12 months. Overall survival was 89.2% at 18 months. Time related survival was 84% at 18 months for the whole group and 88% for the group with CABG or MV repair (Figs. 7 and 8).

Multivariate analysis identified incremental risk factors for death at any time after operation. These included lower postoperative EF ($p < 0.0003$), older age ($p = 0.01$) and concomitant MV replacement ($p < 0.0001$).

The influence of postoperative EF on 18-month survival for a 60-year-old patient without MV replacement is shown in Figure 9, which illustrates a more favorable outlook among patients with a high EF. The combined influences of advancing age and postoperative EF are shown in Figure 10. If the postoperative EF is high, advancing age has little impact on survival. However, if the postoperative EF is low, survival decreases markedly with advancing age.

Concomitant MV replacement among 18 patients was associated with a reduced survival (Fig. 8). Eight patients underwent MV replacement in a center utilizing integrated blood cardioplegia during CABG/MV replacement followed by the open-beating method during patch placement. The two deaths among these eight cases (25%) were not due to low output syndrome. Despite relatively long aortic occlusion times (mean 87 min, range 60 to 140 min), no patient required IABP. By contrast, mortality was 30% among ten patients undergoing MV replacement in centers using cardioplegia-arrest during the entire operation and was predominantly due to low output syndrome. Intraaortic balloon counterpulsation was required in 30% to separate from cardiopulmonary bypass.

Follow-up. Freedom from rehospitalization for CHF at 18 months after operation was 85%. Rehospitalization peaked between two and four months and leveled to 8.8% per year during the 18-month follow-up (Fig. 11). The risk of

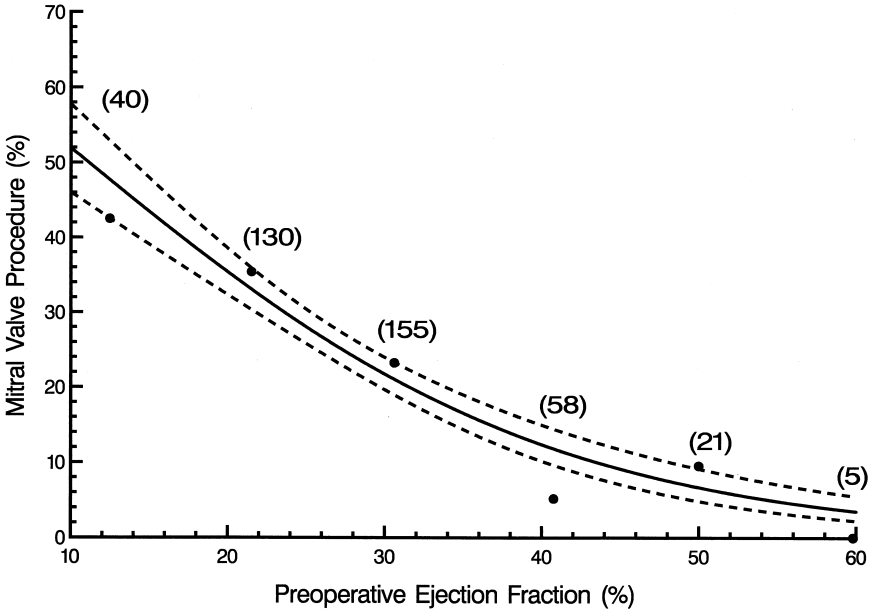

Figure 5. Prevalence of performing a concomitant mitral valve procedure according to preoperative ejection fraction. **Closed circles** represent the observed proportion of patients receiving a mitral valve procedure in roughly 10% increments in ejection fraction. The number of patients in each group is shown for each dot. The **solid line** and its confidence limits are a trend line from logistic regression ($p < 0.0001$).

readmission was relatively insensitive to postoperative EF until it was <30%. (Fig. 12).

Among 277 patients for whom New York Heart Association functional class was reported, 36% were class I, 39% class II, 21% class III and 3% class IV.

DISCUSSION

Ventricular dilation is an adaptive mechanism early after infarction. It maintains stroke volume, but progressive remodeling may become pathologic by its effect on the remote noninfarcted myocardium (21). Myocyte hypertrophy and elongation develop with interstitial fibrosis, which leads to an increasing mass without an increase in wall thickness (eccentric hypertrophy) (22,23). Dilation also distorts the normal fiber angle, which adversely affects systolic torsion (24). Advanced enlargement leads to altered ventricular shape and papillary muscle orientation that restricts mitral leaflet coaptation producing regurgitation

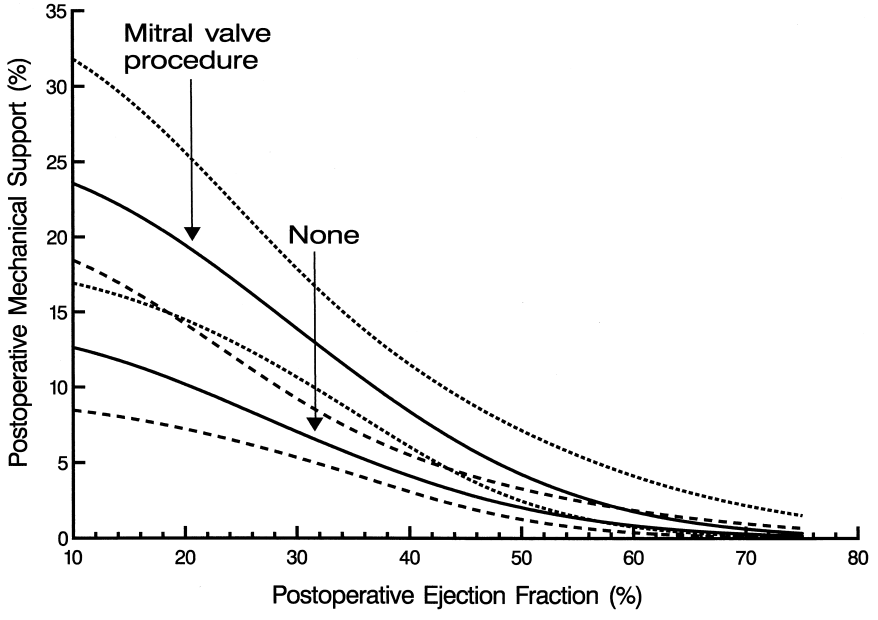

Figure 6. Prevalence of the need for post-SAVER mechanical support according to the level of postoperative ejection fraction and whether a mitral valve procedure (repair or replacement) was performed. The depiction is a nomogram from the multivariable logistic regression analysis.

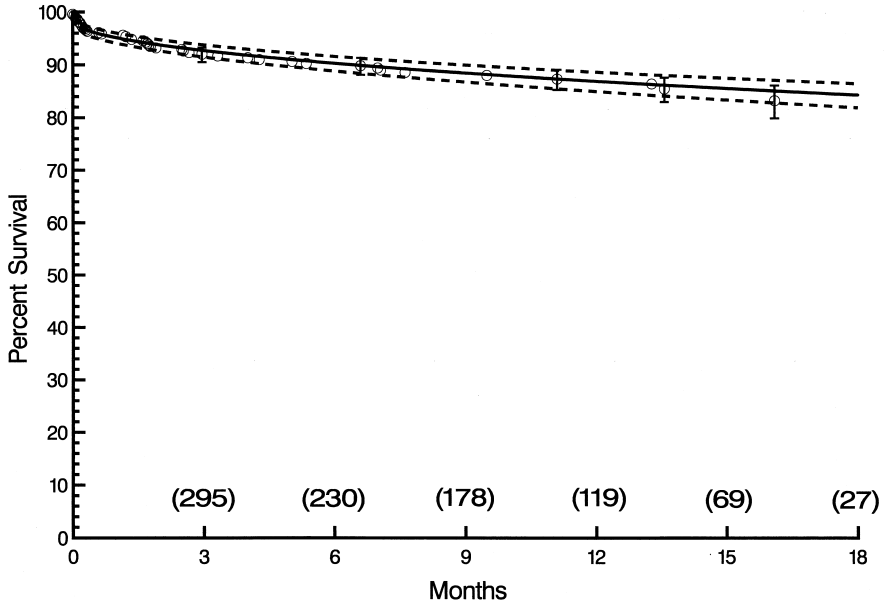

Figure 7. Overall survival after the SAVER operation. **Circles** represent a death and are positioned on the horizontal axis at the time of the death and on the vertical axis according to the Kaplan-Meier estimator. The **vertical bars** are asymmetric confidence limits equivalent to one standard error. The **solid line** enclosed by **dashed line** confidence limits is the parametric survival estimate. The numbers at the foot of the graph represent the number of patients still traced at three-month intervals.

(25). This may occur in experimental models even without mitral annular enlargement (26).

Ventricular dilation is closely linked to risk of death after infarction (27). Successful thrombolysis after infarction can prevent or limit dilation but must occur within hours to achieve significant myocardial salvage and prevent dilation (28,29). The Global Utilization of Streptokinase and t-PA for Occluded Coronary Arteries (GUSTO) I trial examined the effect of early reperfusion on ventricular size using single plane ventriculography at 90 and 180 min into thrombolytic therapy for acute myocardial infarction. The authors found that LVESVI >40 ml/m^2 was associated with an increased rate of hospital CHF and mortality at one year (30). Gaudron et al. (31) studied patients three years after infarction with successful reperfusion and found progressive ventricular dilation in 20%.

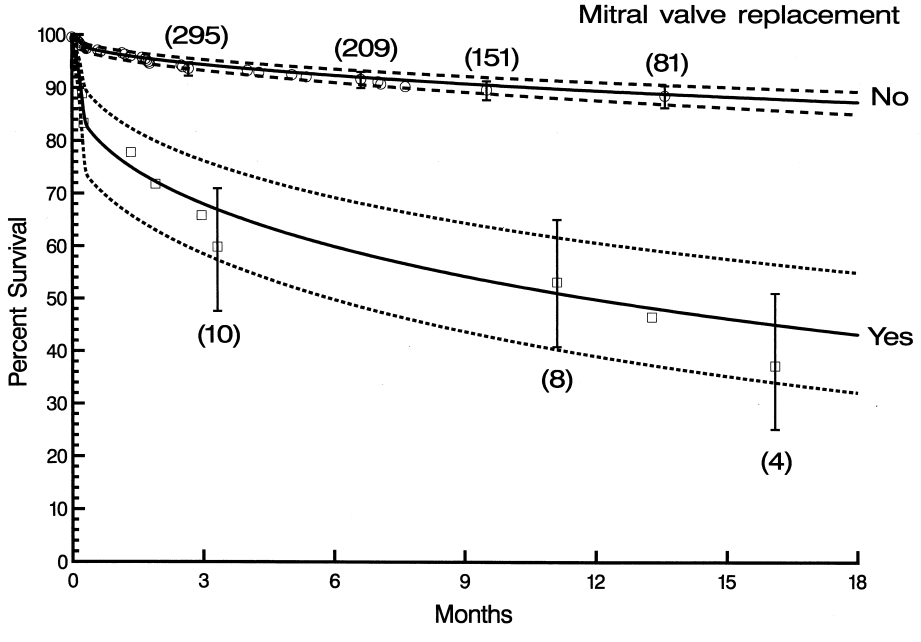

Figure 8. Survival after the SAVER operation according to whether the mitral valve was replaced. In general, the format is as in Figure 3, with **circles** representing patients who did not have mitral valve replacement (but may have had mitral valve repair) and **squares** representing patients with mitral valve replacement. The numbers in parentheses along each curve represent the number of patients still traced beyond that point in time.

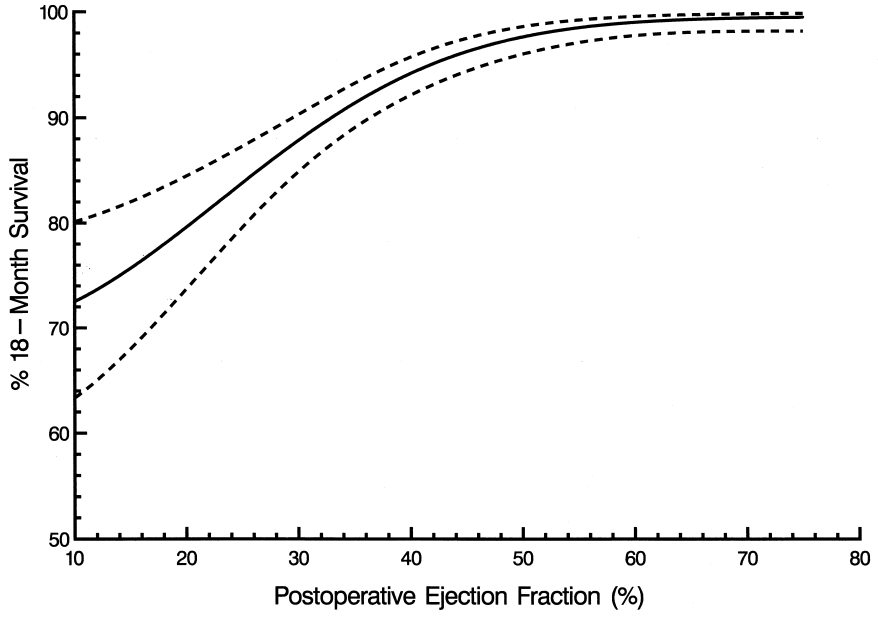

Figure 9. Nomogram of 18-month survival after the SAVER operation from the multivariable analysis of death. To construct this risk-adjusted depiction, age at operation was set at 60 years, and mitral valve replacement was set to "no." Note the expanded vertical axis. The **solid line** is the estimate, and the **dashed lines** are the asymmetric confidence limits.

Preoperative ventricular volume also predicts the prognosis in ischemic cardiomyopathy treated by CABG alone. Yamaguchi et al. (5) observed patients with prior anterior myocardial infarction with EF $<$ 30%. At five years, CHF occurred in 69% of patients with large ventricles (LVESVI $>$ 100 ml/m^2) and in only 15% of patients with smaller ventricles (LVESVI $<$ 100 ml/m^2). Mortality was similarly affected, demonstrating 54% survival in patients with large ventricles compared with 85% among patients with smaller ventricles.

Surgical anterior ventricular restoration decreases wall tension by reducing chamber size (Laplace's law). It attenuates oxygen requirement of the remote muscle, improving the oxygen supply/demand relationship. DiDonato et al. (32) and Dor have shown that volume reduction by infarct exclusion enhances regional systolic function in the myocar-

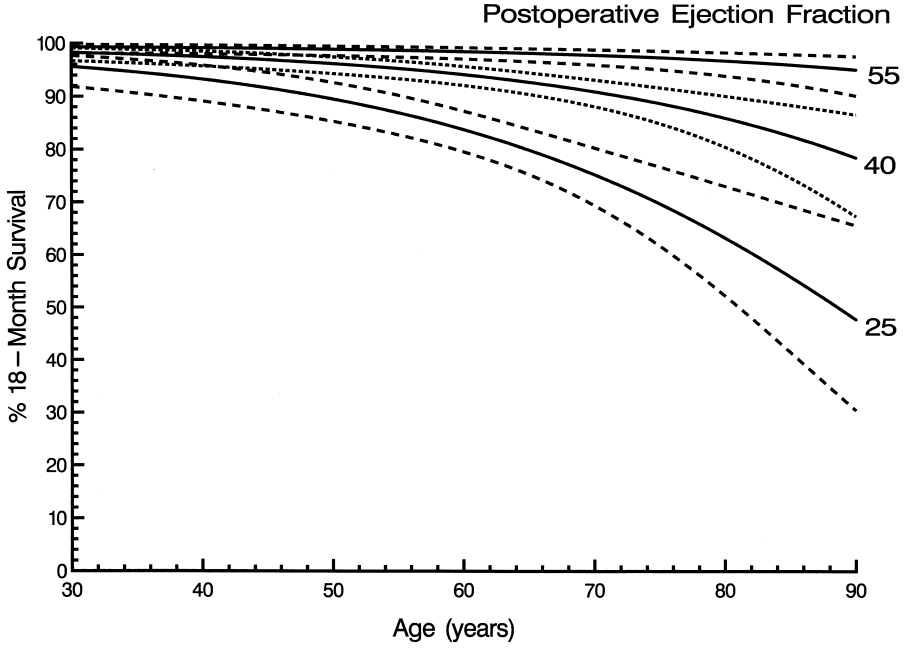

Figure 10. Nomogram of 18-month survival after the SAVER operation according to age and levels of ejection fraction from the multivariable analysis of death. For this depiction, mitral valve replacement was set to "no."

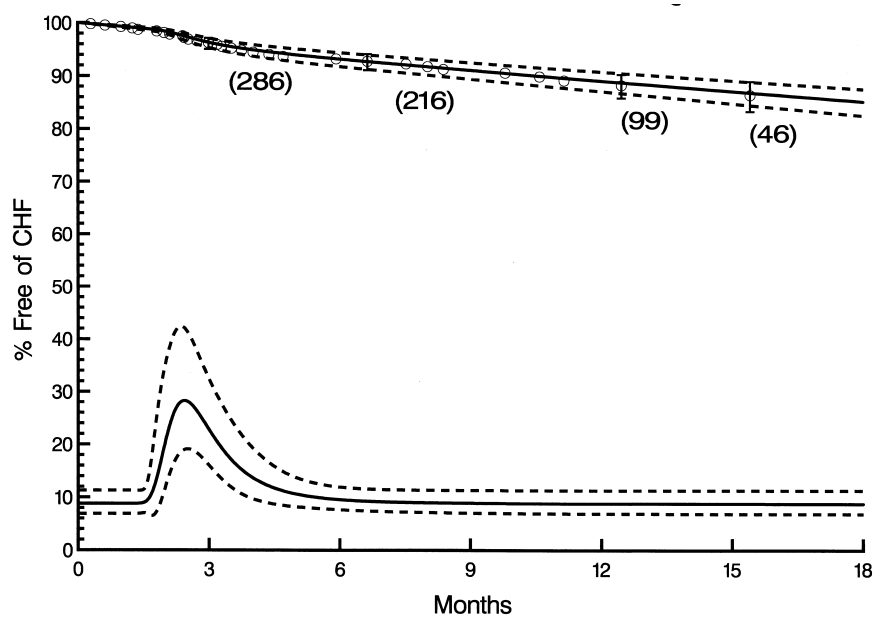

Figure 11. Freedom from rehospitalization for chronic heart failure (CHF) after the SAVER operation. The format of the figure is as for Figures 3 and 4, except that the hazard function (instantaneous risk of rehospitalization for CHF) has been superimposed. It is scaled as % risk of rehospitalization per year.

dium remote from the anterior scar. An additional benefit of volume reduction may be shape alteration, which realigns muscle fiber orientation to allow optimal ejection (33).

The RESTORE group confirmed the feasibility of operating on akinetic scars. Palpation of the open-beating heart distinguished noncontracting akinetic segments that did not collapse during ventricular decompression. Operative and late mortality was low. In this study, average preoperative LVESVI of 109 ml/m^2 was reduced to 69 ml/m^2 postoperatively. After this significant volume reduction, left ventricular systolic function improved. Global EF increased from 29% to 39%. Mechanical support use was uncommon (9%) despite poor preoperative systolic function. At 18 months, 85% of discharged patients had not been readmitted for CHF.

Study limitations. The primary intent of this registry was to confirm Dor's extensive experience and introduce surgeons to the concept of excluding the akinetic ventricle. Although many surgeons used cardioplegia-arrest throughout the procedure, others used the open-beating method of

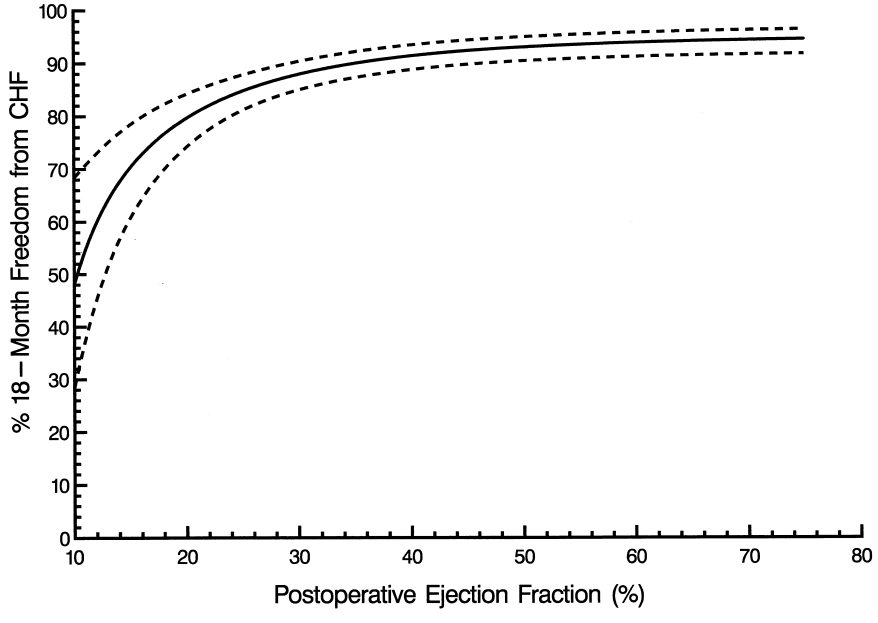

Figure 12. Nomogram of 18-month freedom from rehospitalization for chronic heart failure (CHF) according to postoperative ejection fraction. For this risk-adjusted depiction, age was set at 60 years. The **solid line** is the point estimate, and the **dashed lines** are their confidence limits.

protection during patch placement. Hence, the operations were not precisely duplicated among centers.

Left ventricular end systolic volume index and EF were not obtained in all patients. Follow-up measurements were recorded in ambulatory patients between one and several weeks postoperatively. All volumes were obtained by ventriculography; however, biplane methodology was not used exclusively. Ejection fraction was calculated by echocardiography or ventriculography. Although EF was calculated by the same method for each patient before and after operation, it was not obtained at precisely the same postoperative interval.

Congestive heart failure evaluation was based on clinical assessment alone and provided by the same observer for each patient. The clinical criteria for readmission to the hospital for CHF were not defined.

Patients were not randomized to medical therapy, CABG alone, CABG/mitral procedures or a combination of these procedures with SAVER.

Conclusions. Our multicenter experience in 439 patients validates the safety and efficacy of SAVER and confirms Dor's single center experience in 835 patients with dilated cardiomyopathy after anterior myocardial infarction (34). Surgical anterior ventricular restoration is associated with low operative mortality and infrequent use of mechanical support. Survival at 18 months was encouraging and rehospitalization for CHF was low.

The consequence of ventricular dilation after infarction is detrimental. Our results support the need for randomization of SAVER with medical therapy or CABG alone in postinfarction dilated cardiomyopathy. Furthermore, SAVER early after infarction may prevent late ventricular dilation. The RESTORE group's ongoing experience will further define the indications and optimal methods of restoration.

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